Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 58-62, 64-78, 80, 81, and 100-107 are pending in the application, with claim 58 being the independent claim. Claims 1-57, 63, 79, and 82-99 have been cancelled without prejudice to or disclaimer of the subject matter therein. New claims 101-107 are sought to be added.

Support for the amendment to claim 58 is found *inter alia*, at page 25, paragraphs [0114] to [0115], and page 30, paragraph [0134]. Support for new claim 101 can be found, *inter alia*, at page 12, paragraphs [0051] to [0052], and at page 38, paragraph [0155]. Support for new claims 102-107 can be found, *inter alia*, in the claims as originally filed. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejections under 35 U.S.C. § 112

The Examiner rejected claim 63 under 35 U.S.C. § 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention". *See* Office Action at pages 2-3. Solely in order to advance prosecution, and not in acquiescence of the Examiner's rejections, Applicants have cancelled claim 63. Therefore, this rejection is rendered moot.

In addition, the Examiner also rejected claim 59g under 35 U.S.C. § 112, second paragraph "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention". *See* Office Action at page 12. The Examiner stated that claim 59g refers to a polypeptide comprising a transmembrane domain and that transmembrane domains are not soluble proteins. Applicants note that claim 59g refers to a "polypeptide comprising an Sp35 Ig domain, but lacking an Sp35 LRR domain, an Sp35 basic region, a transmembrane domain, and a cytoplasmic domain" (emphasis added). Therefore, claim 59g refers to a polypeptide that lacks the transmembrane domain. Therefore, Applicants respectfully request that this rejection is withdrawn.

Rejections under 35 U.S.C. § 102

Osada Does Not Anticipate the Present Claims

Claims 58, 59, 64-66, 69, and 70 are rejected by the Examiner under 35 U.S.C. § 102(b) "as being anticipated by Osada *et al.* (2001; Assignment of 118 novel cDNAs of cynomolgus monkey brain to human chromosomes. *Gene. 275*: 31-37)" ("Osada"). *See* Office Action at page 4.

Osada is cited as disclosing a nucleic acid encoding a protein that differs from instant SEQ ID NO:2 at a single amino acid (Ser527Pro). According to the Examiner, Osada thus discloses "a nucleic acid *comprising* (reads on full-length LINGO-1) nucleic acid encoding the soluble fragment of 454-458 of SEQ ID NO:2." *Id.*, emphasis in original.

Applicants have amended the claims to clarify that expression of the claimed polynucleotide in a cell produces a soluble polypeptide. Osada is cited as disclosing the polynucleotide sequence of a brain-specific cDNA from cynomolgus monkey that is predicted to encode a 614 amino acid protein. The protein contains a transmembrane domain and is not a soluble fragment of SEQ ID NO:2. Thus, expression of the polynucleotide of Osada in a cell would not produce a soluble polypeptide.

Furthermore, the pending claims require that the soluble polypeptide is capable of decreasing inhibition of axonal growth of a central nervous system neuron. Osada is directed to assigning cynomolgus monkey brain cDNAs to human chromosomes and does not teach or even suggest that any portion of the disclosed polypeptide is capable of decreasing inhibition of axonal growth of a central nervous system neuron.

Under 35 U.S.C. § 102, a claim can only be anticipated if every element in the claim is expressly or inherently disclosed in a single prior art reference. *See Kalman v. Kimberly Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983), cert. denied, 465 U.S. 1026 (1984). Because Osada does not expressly or inherently disclose either a polynucleotide wherein expression of said polynucleotide in a cell produces a soluble polypeptide or a soluble polypeptide that is capable of decreasing inhibition of axonal growth of a central nervous system neuron, Osada does not disclose every element of the presently claimed invention. Hence, under *Kalman*, this reference cannot support a rejection of the claims as currently amended under 35 U.S.C. § 102(b).

In view of the foregoing remarks, Applicants respectfully assert that Osada does not anticipate claims 58, 59, 64-66, 69, and 70 as amended and does not anticipate new

claims 101-107. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) over Osada therefore is respectfully requested.

Jacobs Does Not Anticipate the Present Claims

Claims 58-78, 80, and 100 are rejected by the Examiner under 35 U.S.C. § 102(b) "as being anticipated by Jacobs *et al.* (1998; USP 5,707,829)" ("Jacobs"). *See* Office Action at page 6.

Jacobs is cited as disclosing a 133 amino acid sequence (SEQ ID NO:6) and a polynucleotide encoding that sequence (SEQ ID NO:5). Amino acids 66-69 of Jacob's SEQ ID NO:6 correspond to amino acids 454-458 of SEQ ID NO:2 of the present application. According to the Examiner, Jacobs thus discloses a nucleic acid encoding a fragment of instant SEQ ID NO:2, wherein that fragment is amino acids 454-458 of SEQ ID NO:2. *Id.* The Examiner further states that because the elected amino acid sequence 454-458 of SEQ ID NO:2 is encoded by the sequence of Jacobs, the sequence of Jacobs must have the property of decreasing the inhibition of axonal growth in a CNS neuron.

Applicants respectfully disagree. First, in order to advance prosecution, and not in acquiesce of the rejections, claim 59 has been amended to recite soluble polypeptides that comprise larger portions of SEQ ID NO:2 than that disclosed in Jacobs. In addition, new claim 101 requires that the polypeptide consists of the amino acids 454-458 or 453-458 of SEQ ID NO:2. Therefore, at the very least, claims 59 and 101, and claims that depend therefrom, are not anticipated by Jacobs.

Furthermore, Jacobs does not anticipate claim 58 because, contrary to the Examiner's statement, the protein of SEQ ID NO:6 does not have the property of

decreasing the inhibition of axonal growth of a central nervous system neuron. According to Jacobs, the protein of SEQ ID NO:6 has homology to monocyte and other chemoattractant proteins and is expected to share at least some activities with these proteins. Jacobs, col. 5, lines 11-19. Monocytes and other chemoattractant proteins regulate cell trafficking, not axonal growth. In addition, monocytes and other chemoattractant proteins regulate immune system cells, not neuronal cells. Thus, Jacbos does not even suggest that the protein of SEQ ID NO:6 decreases inhibition of axonal growth of central nervous system neurons.

In addition, the sequence described by Jacobs corresponds to the chemokine (C-C motif) ligand 21a (serine) protein in mouse (NCBI Accession number NP_035254). The murine chemokine (C-C motif) ligand 21a protein ("CCL21a"), which differs from chemokine (C-C motif) ligand 21a (serine) only at the single amino acid Ser64Leu, has been further characterized by several other groups including Hedrick *et al.* (*J. of Immunology 159*: 1589-1593 (1997)) ("Hedrick"). Hedrick shows that the sequence of CCL21a aligns with that of other β-chemokines such as human MIP-3α. Hedrick, Figure 1. The three-dimensional structure of such chemokines has previously been determined. The nuclear magnetic resonance (NMR) structure of murine MIP-3α is shown in Perez-Canadillas *et al.* (*J. of Biol. Chem. 276*: 288732-28379 (2001)) ("Perez-Canadillas"; Exhibit 1). Perez-Canadillas states that murine MIP-3α exhibits the same structure previously described for other chemokines: a three-stranded β-sheet and an overlying α-helix. Abstract. This indicates that amino acids 66-69 in the context of Jacob's SEQ ID NO:6 are located in this three-stranded β-sheet plus overlying α-helix three-dimensional chemokine structure.

In contrast, as indicated in the present specification, amino acids 454-458 in the context of SEQ ID NO:2 of the present application are located in a loop of an Ig domain. Page 38, paragraph [0155]. The Ig domain has also been studied and consists of a five-strand β-sheet. A comparison of the ribbon diagrams of the structure of the Ig domain, as shown in Figure 3D of Mosyak *et al.* (*J. of Biol. Chem. 281*:36378-36390 (2006)) (Exhibit 2), and the chemokine domain, as shown in Figure 6 (left) of Perez-Canadillas, reveals that the amino acids 66-69 in Jacob's SEQ ID NO:6 and amino acids 454-458 in SEQ ID NO:2 of the present application are found in entirely different three-dimensional structures and therefore would not have the same functional features. This observation is confirmed by the fact that CCL21a and SEQ ID NO:2 of the present invention have been shown to have different functional features. Hendrix demonstrates that CCL21a regulates immune cells, and the present specification demonstrates that SEQ ID NO:2 regulates neuronal cells.

Thus, Applicants submit that the full-length protein of SEQ ID NO:6 of Jacobs does not have the property of decreasing the inhibition of axonal growth of a CNS neuron, despite the fact that it contains the elected amino acid sequence. In addition, Jacobs does not teach any specific fragments of SEQ ID NO:6 at all. As a result, Jacobs does not teach or suggest any soluble polypeptides that are capable of decreasing inhibition of axonal growth of a central nervous system neuron. Since Jacobs does not teach a polypeptide of SEQ ID NO:2 that is capable of decreasing inhibition of axonal growth of a central nervous system neuron, Jacobs does not expressly or inherently disclose every element of the presently claimed invention. Hence, under *Kalman*, this reference cannot support a rejection under 35 U.S.C. § 102(b).

In view of the foregoing remarks, Applicants respectfully assert that Jacobs does not anticipate claims 58-78, 80, and 100 and does not anticipate new claims 101-107. Thus, reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) over Jacobs therefore is respectfully requested.

Rejections under 35 U.S.C. § 103

The Present Claims are Not Obvious in view of Osada

Claims 58, 69, 70, 71, 72, 80, and 100 are rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Osada. *See* Office Action at page 6.

The USPTO has recently published guidelines for Examiners in determining whether claims are non-obvious under the *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007) holding. 72 FR 57526. While the Office sets forth a number of rationales by which a determination of obvious may be made, a common thread throughout requires that the prior art, in combination with the knowledge ascribed to the person of ordinary skill in the art, provide sufficient information to make the claimed invention fully and easily predictable.

As described above, Osada is cited as disclosing the cynomolgus monkey LINGO-1 polypeptide and states that the protein contains an immunoglobulin domain, a leucine rich repeat, a leucine rich repeat N-terminal domain, and a leucine rich repeat C-terminal domain. *See* Tables 1 and 2. The polypeptide also contains a transmembrane domain and therefore is not a soluble protein. Osada, does not, however disclose the sequence of any fragments of the cynomolgus monkey LINGO-1 protein. Furthermore,

Osada does not describe any function of the protein at all. Thus, one of ordinary skill in the art would have neither the motivation nor the knowledge to make a soluble polypeptide that decreases the inhibition of axonal growth of a central nervous system neuron.

Thus, for at least these reasons the Examiner has not established a *prima facie* case of obviousness. Therefore, Applicants respectfully request that the rejection of claims 58, 69, 70, 71, 72, 80, and 100 under 35 U.S.C. § 103(a) over Osada are reconsidered and withdrawn.

The Present Claims are Not Obvious in view of Jacobs

Claims 58-78, 80, and 100 are rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Jacobs. *See* Office Action at page 10. Specifically, the Examiner asserted that art anticipating a nucleic acid encoding amino acids 454-458 of SEQ ID NO:2 renders obvious all of the variants listed in the claims.

Applicants respectfully disagree. In order to advance prosecution, and not in acquiescence to the rejection, Applicants have amended claim 59 to recite fragments that encompass larger portions of SEQ ID NO:2 than the amino acids described by Jacobs. Applicants have added claim 101 directed to fragments that consist of the recited fragments of SEQ ID NO:2.

Jacobs is cited as disclosing a 133 amino acid sequence and does not identify the specific fragment that corresponds to amino acids 454-458 of SEQ ID NO:2 of the present specification. Applicants submit that one of ordinary skill in the art would certainly not have any motivation, in view of Jacobs, to modify the polypeptide of SEQ

ID NO:6 in Jacobs to arrive at sequences of claim 59 or claim 101. Therefore, at the very least, claims 59 and 101 are not rendered obvious by Jacobs.

In addition, Applicants emphasize that all of the present claims require that the polypeptide decreases inhibition of axonal growth of a central nervous system neuron. As described above, the protein of SEQ ID NO:6 in Jacobs does not decrease inhibition of axonal growth of a central nervous system neuron. Furthermore, even if one of skill in the art were motivated to modify the polypeptide of SEQ ID NO:6 in Jacobs, Jacobs does not provide any motivation to select a fragment that corresponds to amino acids 454-458 of SEQ ID NO:2 of the present specification. Therefore, one of skill in the art would not have had any suggestion to modify the polypeptide of SEQ ID NO:6 in Jacobs to arrive at the claimed invention.

For at least these reasons the Examiner has not established a *prima facie* case of obviousness. Therefore, Applicants respectfully request that the rejection of claims 58-78, 80 and 100 under 35 U.S.C. § 103(a) over Jacobs are reconsidered and withdrawn.

Statement of the Substance of the Interview

Applicants thank Examiner Karen C. Carlson for her time in participating in a personal interview with Elizabeth J. Haanes and Cynthia L. DeRenzo on September 17, 2009 to discuss the outstanding Office Action. During the interview, Applicants and the Examiner discussed the 35 U.S.C. §§ 102(b) and 103(a) rejections.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

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